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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/630,968

07/31/2003

John J. Rossi

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6449

7590

03/07/2008

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EXAMINER

SHIN, DANA H

ART UNIT

PAPER NUMBER

1635

NOTIFICATION DATE

DELIVERY MODE

03/07/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No. 10/630,968	Applicant(s) ROSSI ET AL.	
	Examiner DANA SHIN	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 17-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 17-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 4, 2008 has been entered.

Status of Claims

Currently, claims 1-9 and 17-23 are pending and under examination on the merits.

Response to Arguments

Applicant's arguments, see pages 5-7, filed on February 4, 2008, with respect to the rejection(s) of claim(s) 1-9 and 17-23 under 35 U.S.C. §103(a) have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made as below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 17-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Engelke et al. (US 2003/0148519 A1) in view of Livache et al. (citation of record).

The claims are drawn to a PCR-based amplification method for producing a U6 promoter-containing siRNA expression cassette, comprising treating one strand of the promoter sequence with an oligonucleotide primer complementary to the 5' end of the promoter sequence, treating the other strand of the promoter sequence with an oligonucleotide primer complementary to the 3' end of the promoter sequence, wherein the primer further comprises a sequence encoding either strand of an siRNA molecule and a terminator sequence in an amplification reaction mixture, wherein the method further comprises repeated amplification steps to produce an amplified promoter-containing siRNA expression cassette, the method further comprising the step of transfecting mammalian cells with the siRNA expression cassette.

Engelke et al. teach a U6 promoter-containing siRNA expression cassette further comprising a transcription termination sequence, which is constructed by molecular cloning technology and a method of transfecting the cassette into mammalian cells. See Figure 1A and

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paragraphs 0017-0020, 0088-0091, 0124-0126, 0140. They teach that synthesis of siRNA molecules is expensive and the naked siRNA molecules do not achieve long-term expression in the appropriate subcellular location. See paragraphs 0008, 0132. They teach that to remedy the problems associated with the cost of synthesizing siRNA molecules and the short-term expression of such naked siRNA molecules in appropriate location of cells, one of ordinary skill in the art can make a recombinant expression vector construct wherein a U6 promoter expresses siRNA molecules in mammalian cells. See paragraphs 0008, 0132, 0134-0138. They teach that PCR is a method for amplifying a segment of a target sequence without cloning or purification, wherein the method comprises a step of introducing two oligonucleotide primers to a reaction mixture containing the desired target sequence, wherein the two oligonucleotide primers are complementary to their respective strands of the double stranded target sequence. They teach that the steps of denaturation, primer annealing, and polymerase extension can be repeated as many times as possible to obtain a high concentration of an amplified segment of the desired target sequence. See paragraphs 0073-0076. Note that all of the pertinent teachings of Engelke et al. described herein are adequately supported by the disclosure of their provisional application filed on November 14, 2001. Engelke et al. do not teach that the U6 promoter-containing siRNA expression cassette is constructed by PCR-amplification method.

Livache et al. teach a method of producing a double-stranded RNA expression cassette containing a promoter via a PCR-based method by integrating oligonucleotide primers that are complementary sequences that encompass the sequence of a promoter and the target sequence, wherein the duplex RNA has a defined length. They teach that such method is rapid and inexpensive.

It would have been obvious to one of ordinary skill in the art at the time the invention was made, which is declared to be prior to April 15, 2002 by applicant's filing of the declaration under 37 CFR 1.131, to use the PCR-amplification method of Livache et al. to make the U6 promoter-containing siRNA expression cassette of Engelke et al.

One of ordinary skill in the art would have been motivated to replace the molecular cloning method of constructing a U6 promoter-containing siRNA expression cassette of Engelke et al. with the PCR-based amplification method of Livache et al., because Engelke et al. taught that PCR is a method for amplifying a segment of a target sequence without cloning or purification by utilizing two oligonucleotide primers that are complementary to their respective strands of the double stranded target sequence and because Livache et al. taught that double-stranded RNA expression cassette constructs can be made via a PCR-based amplification method by utilizing oligonucleotide primers that are complementary sequences that encompass the sequence of a promoter and the target sequence. Since an siRNA molecule-containing expression vector driven by a U6 promoter was desired in the art compared to naked siRNA molecules which are expensive to synthesize and have a short life span in cells, as taught by Engelke et al., one of ordinary skill in the art would have been motivated to try a different methodology of constructing such expression vector other than the cloning/purification methods used by Engelke et al. Since PCR was a well-known method to amplify target gene sequence as evidenced by Engelke et al. and Livache et al., and since PCR was also known to produce a double-stranded RNA expression cassette both rapidly and inexpensively as taught by Livache et al., one of ordinary skill in the art would have been motivated to produce the vector of Engelke et al. by employing a PCR-based amplification method in place of the cloning/purification method. Since

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all of the skills and knowledge required to arrive at the claimed invention were within the technical grasp of one of ordinary skill in the art, and since there were beneficial incentives in replacing the cloning technology of Engelke et al. with the PCR-based amplification technology (e.g., saving both time and money) as recognized by Livache et al., one of ordinary skill in the art would have had a reasonable expectation of success and reasons to pursue the claimed invention at the time the invention was made. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner, Art Unit 1635